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UNITED STATES DEPARTMENT OF AGRICULTURE
AGRICULTURAL BIOTECHNOLOGY RESEARCH ADVISORY COMMITTEE
CLASSIFICATION AND CONFINEMENT WORKING GROUP
MINUTES OF MEETING
May 21, 1991

Dr. John Kemp, Chair, called this meeting of the Classification and Confinement Working Group (the Group) of the Agricultural Biotechnology Research Advisory Committee (ABRAC) to order at 9:05 a.m. The Group members in attendance were Dr. Kemp, Dr. Anne Vidaver, Dr. Ann Sorensen, Dr. Bennie Osburn, and Dr. William Witt. Office of Agricultural Biotechnology (OAB) staff in attendance included Dr. Daniel Jones, Mr. Paul Stern, and Ms. Maryln Cordle. Dr. Marshall Phillips, Agricultural Research Service (ARS), and Dr. Sue Tolin, Virginia Polytechnic Institute and State University, were also present.

Introductory Remarks

Dr. Kemp described the purpose of the meeting with respect to the "Proposed Guidelines for Research Involving the Planned Introduction into the Environment of Organisms with Deliberately Modified Hereditary Traits" (hereafter referred to as the Guidelines) previously published in the Federal Register (56 FR 4134, February 1, 1991). He said the major goal will be to improve the Guidelines in response to public comments and to recommend action to the U.S. Department of Agriculture (USDA) for finalization of the Guidelines. He suggested that the morning session be devoted to analyzing the Guidelines themselves, and that the afternoon session concentrate on re-analyzing the Guidelines in light of public comments. He noted that Mr. Stern's analysis of the public comments would be very helpful during the afternoon session.

The Group accepted the agenda and proceeded with the morning analysis of the Guidelines. Dr. Sorensen asked if the purpose of the morning session was to see if the Group was comfortable with the Guidelines, and whether prior knowledge of public comments would bias the group's deliberations. Dr. Kemp responded that such bias was a concern, and that the morning session was designed to deal with that.

Dr. Vidaver asked if, after reviewing the Guidelines in light of the public comments, the two analyses would be integrated. Dr. Kemp responded affirmatively, adding that the Group could make both general and specific recommendations on the Guidelines for consideration by the entire ABRAC. He noted that many of the comments addressed very specific issues.

Dr. Sorensen asked if the U.S. Department of Agriculture (USDA) would publish responses to the comments. Dr. Jones answered that USDA had to respond to the comments in some fashion, but that the responses would probably be tailored to groups of

comments rather than address each individual letter. He invited the Group to suggest ways to respond to the comments and said that responding to the comments would take several months.

Dr. Jones also reported that the USDA Guidelines Implementation Committee had met three or four times since the Guidelines were published and that it was drafting recommendations.

Dr. Vidaver asked which agencies were members of the Implementation Committee. Dr. Jones replied that the members consisted of the Agricultural Research Service (ARS), the Cooperative State Research Service (CSRS); the Animal and Plant Health Inspection Service (APHIS); the Forest Service (FS); the Office of Agricultural Biotechnology (OAB); and the immediate office of the Assistant Secretary for Science and Education. He noted that while most of the participating agencies are those which perform or fund research, regulatory agencies were participating because their activities also affect the Guidelines.

Dr. Phillips introduced himself and said that he was in town for a meeting of the American Chemical Society. Dr. Jones and Dr. Kemp noted that Dr. Phillips had previously served a detail with OAB and had offered himself as a resource to the Group. Dr. Jones related that Dr. Fred Gould had been contacted about the meeting, but was out of the country and thus could not attend.

Review of the Four Steps

Dr. Kemp invited the Group to begin analyzing the Guidelines. He reviewed the Guidelines' step-by-step process for selecting the conditions for safely performing biotechnological research. These steps are:

1. Determine the level of safety concern for the parent organism;

2. Determine the effect of the genetic modification on the level of safety concern;

3. Determine the level of safety concern for the modified organism; and

4. Determine the level of confinement appropriate to the level of safety concern for the modified organism.

Dr. Kemp asked if this scenario was an appropriate way to determine a final confinement strategy. Dr. Vidaver responded by asking if certain terms such as "parental organism" needed to be defined. Dr. Kemp suggested that the Group begin listing such terms and try to define them.

Definitions of Terms

The first term to be addressed was "parental organism," defined by Dr. Kemp as the organism to be modified. Dr. Vidaver suggested that the parental organism is the organism that you are working with that is to be modified. Dr. Jones wondered if the word "parental" would cause confusion, and noted that the previous term had been "unmodified organism." Dr. Vidaver said that unless there was an overriding concern, she would be inclined to say that the parental organism is the organism a researcher starts with in modifying hereditary traits. Dr. Osburn agreed with that definition, and suggested its inclusion with the first use of the term in the Guidelines. Dr. Kemp said there would be no problem with that and suggested that the whole ABRAC address some of the other terms, such as the actual title of the Guidelines.

Mr. Stern said that three of the comments expressed confusion over the use of the term "parental organism" when dealing with recombinant technology. Dr. Kemp suggested that examples that carried through from parental to modified organism would clear up such confusion. Dr. Sorensen asked if the confusion is whether the parental organism is the organism from which the DNA originates or the organism to be modified. Dr. Kemp replied that the Group seemed to agree that the parental organism is the unmodified, starting organism.

Product versus Process

Dr. Sorensen cited some unease in the agricultural community over whether the Guidelines were intended to regulate the products of biotechnology or the process that creates those products. Dr. Kemp said that the four steps tried not to address the process, and that they deal with the safety of the product. Dr. Sorensen agreed, but noted that some commentators didn't see the Guidelines that way. Mr. Stern said that only a handful of commentators expressed concern that the Guidelines were based on process rather than product.

Dr. Kemp noted that some commentators expressed the view that the exclusions mentioned in the Guidelines are based too much on process considerations. Dr. Vidaver replied that the steps could be performed on any product, and thus were independent of the process.

Ms. Cordle said that the product-versus-process issue is basically a scope issue. She added that some comments claimed the Guidelines contain too few examples of determining the level of safety concern, and dealt only with parental organisms, not the modified organisms.

Five Attributes and the Definition of "Accessible Environment"

Dr. Kemp invited the Group to analyze the five attributes described in Section VI of the Guidelines, relating to safety concern for the parent organism.

Dr. Vidaver asked the Group to clarify the term "accessible environment." Dr. Kemp asked if the term meant any possible environment where the organism could end up, or if the definition should be more pragmatic. Dr. Sorensen suggested that the definition be "the environment accessible to the organism in the absence of confinement." Dr. Kemp called for pragmatism in defining this term.

Dr. Tolin noted that in small-scale testing, organisms are confined inherently. She suggested that accessible environment be defined as the environment accessible to the organism in the absence of additional confinement beyond its natural biology and environment.

Ms. Cordle asked if it would be appropriate for the definition to mention natural biological barriers, natural climatic barriers, and standard agricultural practices such as tillage, etc.

Dr. Kemp replied that the answer depends on the specific case, but that the question is what the organism would do in the absence of additional confinement. He added that a researcher needs to look at the specific conditions of his or her experiment and see what the organism might do without confinement. Dr. Tolin cited the Guidelines' examples as showing that levels of safety concern could vary with location.

Dr. Vidaver noted that researchers normally use some level of confinement for organisms in field tests, even though this was not explicitly recognized in the Guidelines.

Dr. Kemp asked if the second attribute, the organism's potential to establish itself in the accessible environment, should be interchanged with the first attribute, the organism's pest/pathogen status and potential in the accessible environment. Dr. Tolin said that the term "accessible environment" needed to be moved or modified so that it would be consistent with what is said earlier in the Guidelines.

Dr. Witt suggested that the accessible environment deal with the absence of routine confinement. Dr. Vidaver agreed that a modifier to confinement such as routine or standard might be needed.

Dr. Kemp expressed concern that if the term "accessible environment" is defined too closely, the Guidelines effectively would be telling experts how to perform field trials.

Dr. Osburn said one purpose of the Guidelines was to educate non-experts. Dr. Kemp asked Mr. Stern what non-experts' comments were. Mr. Stern said that no major concerns about defining the accessible environment were stated, but observed that the length of the group's discussion of the issue could reflect a need to clarify the term.

Dr. Kemp summarized the sense of the Group as follows: At the end of the first sentence under VI, Step 1, insert the expression "See VI-A" referring to the definition of the "accessible environment." The second sentence will end with a period after "other organisms in that environment." Delete the expression "accessible to it in the absence of confinement" and resume with "The attributes which should be considered are."

With regard to the description of the five attributes, Dr. Kemp recommended and the Group agreed to interchange Sections VI-B-1 and Sections VI-B-2. The Group agreed that no further changes to the attributes were needed.

Safety Levels

The Group then turned to Appendix 1 of the Guidelines, which gives examples of determinations of levels of safety concern for parental organisms. Dr. Kemp asked if those examples were accurate, and if the reader could see how the Guidelines determined the levels of safety concern for each example.

Dr. Sorensen noted that the public commented on all of the examples. Dr. Vidaver asked where in the Guidelines the reader is advised that the level of safety concern is not derived from a sum, mean, minimum or maximum. Ms. Cordle replied that such advice is located in Section VI-D. Dr. Vidaver suggested that the advice be reiterated in Appendix 1 itself, or in a footnote to Appendix 1, Table 1. Mr. Stern suggested that the footnote be appended to the "Overall Level of Safety Concern" column of Appendix 1, Table 1.

Dr. Sorensen asked if the present draft of the Guidelines contains too many levels of safety concern. Dr. Kemp suggested that the five safety levels might be reduced to three safety levels of low, moderate, and high concern.

Dr. Tolin noted that the current draft of the Guidelines detailed the extreme levels of safety concern at either end of the spectrum, but did not detail the middle levels (levels 2, 3, and 4) similarly. Dr. Sorensen agreed, and added that attempting to distinguish among the three middle levels was a problem.

Mr. Stern said that 25 of the public comments addressed the determination of safety concern. Of the 25, only 5 were

positive. The rest wanted the five levels compressed into three levels, or more detailed descriptions of levels 2, 3, and 4.

Dr. Kemp suggested that the group revisit the issue of condensing the five levels of safety concern to three, and pay particular attention to how such action would affect Table 1 of the Guidelines.

After some discussion, Dr. Kemp recommended that the five levels of safety concern be compressed into three levels. Specifically, he suggested that in Section VI-D of the Guidelines, safety levels 2, 3, and 4 be combined into one level of concern. The new levels of safety concern would be as follows:

Level 1: No concern about safety.

Level 2: Some concern, but manageable.

Level 3: High level of concern which is not manageable.

Dr. Vidaver asked if by compressing the safety levels, precision would be sacrificed for the sake of greater simplicity. Dr. Kemp responded by suggesting that the group look at Appendix 1, Table 1.

Dr. Kemp noted that the first example, the cow, would present no problem; the safety concern would remain at level 1. The same would be true with foot-and- mouth disease: the safety concern would remain at the highest possible level (level 3 in the proposed system).

Mr. Stern noted that one reason for the earlier agreement on five safety levels was that oversight mechanisms were being considered, but that the voluntary nature of the Guidelines might make fewer safety levels more appropriate.

Dr. Kemp noted that different kinds of confinement enable researchers to manage the three middle levels of safety concern. Dr. Vidaver said that within an intermediate level (such as the new level 2), there could still be different levels of intermediate confinement, and asked for a more detailed definition of the term "intermediate." Ms. Cordle said that a document entitled "Good Developmental Practices for Small-Scale Field Research with Genetically Modified Plants and Microorganisms" (GDP), by the Organization for Economic Cooperation and Development (OECD) might have language that would help.

Dr. Kemp asked where bacteria and rapeseed would appear in the new, more compressed system, and decided that level 2 would apply to both. He then asked where the Africanized honeybee would appear. Dr. Sorensen noted that Africanized honeybees, though feared, are in the United States and are used for

pollination in South Africa. Dr. Kemp asked if a better insect example might be available.

Types of Genetic Modification

The Group then looked at the types of genetic modification dealt with in the Guidelines. Type 1 modifications decrease the level of safety concern for the modified organism; Type 2 has no effect on the level of safety concern; and Type 3 modifications increase the level of safety concern. Dr. Osburn suggested combining Types 1 and 2, but Dr. Kemp expressed concern that such a combination would eliminate the possibility of lowering the safety concern through modification. The group decided to leave the three types of modification unchanged.

Discussion of Process-Oriented Language

Dr. Kemp asked whether the term "insertion of nucleic acid" in Section VII-C-1 is too geared toward the process rather than the product of genetic modification. He asked whether the word "genes" should be substituted for "nucleic acid." He noted that genetic modifications can occur in other ways besides insertion of nucleic acid into the parent organism.

Dr. Vidaver expressed more concern with the phrase "not well understood" in Section VII-C-1, and with Section VII-C-2.

Mr. Stern noted that the public comments suggested that the public was not especially concerned with this issue, but Ms. Cordle reported that there was considerable concern at the policymaking levels of government on the process versus product issue.

Dr. Kemp asked Ms. Cordle to draft a revision for Section VII that is more process neutral and resolves the concern raised by Dr. Vidaver.

Level of Safety Concern for the Modified Organism

Dr. Kemp noted that Section VIII of the Guidelines would have to be rewritten if the proposed compression of safety levels from five to three was accepted. He suggested the following modifications to Table 1 in light of the proposed compression of safety levels:

Table 1. - Determination of the Level of Safety Concern for the Modified Organism

Level of safety concern for the parental organism	Level of safety concern for modified organism: Type 1 Modification	Type 2 Modification	Type 3 Modification
Level 1	1	1	2 or 3
Level 2	1	2	3
Level 3	1 or 2	3	3

Ms. Cordle noted that the original five categories had been devised in order to differentiate among levels of management needed. She suggested that the new levels of safety concern be tied both to risk and risk manageability. Dr. Kemp asked Ms. Cordle to draft definitions of all three safety levels for review by the Group.

Dr. Kemp then turned to the confinement protocols as described in Section IX-C. He suggested that with the compression of the number of levels of safety concern from 5 to 3, there really was only one confinement protocol beyond confinement associated with good agricultural practice. He suggested that the group discuss confinement further after lunch.

The Group recessed for lunch at 12:30 p.m., and reconvened at 1:43.

Confinement Protocols

Dr. Kemp asked how the new three levels of safety concern would affect the Guidelines' confinement levels. Dr. Sorensen replied that the new scenario really left only one level of confinement beyond good agricultural practice. Dr. Kemp agreed, saying that the first level of confinement was good agricultural practice, and that the second level of confinement consisted of more stringent levels -- in effect, Section IX-C-2 of the Guidelines.

Dr. Kemp went on to explain that the new second confinement level would integrate the old confinement levels 2, 3, and 4. He added that the second confinement level should require good practice plus sufficient confinement to reduce the level of safety concern down to the equivalent of safety level 1.

Dr. Sorensen pointed out that safety level 1, as discussed previously, would apply to organisms that are safe even if not confined, and she questioned whether the concept of reduction to

safety level 1 would be correct. Dr. Kemp said level 2 confinement should reduce the risk of an experiment to the equivalent of level 1 corresponding to no significant impact. Dr. Vidaver pointed out that effects of modification could be positive and that confinement is intended to reduce negative concerns.

Dr. Vidaver cautioned that careful language would be needed in defining each confinement level. For example, would confinement level 2 be used to ensure that the impact of a modification would not be significant, or that such modification would be beneficial? Dr. Kemp agreed, and added that the group needed to be sure that the new, modified organism did not reverse any of the parental organism's attributes, and that confinement would be designed to reduce risk. Dr. Osburn supported the concept, but cautioned that the wording needed to be right in order to achieve both precision and streamlining.

Dr. Kemp suggested that the group turn to Section IX-B of the Guidelines on confinement measures. He saw no problems with the five types of confinement measures described, and he expressed the view that they would still fit in the streamlined version of the Guidelines. He then asked what should be done about Appendix 2.

Dr. Vidaver asked if the Guidelines mention that good agricultural practices normally include some kind of confinement. Dr. Sorensen suggested that several lines could be added to specify that practice. Dr. Kemp noted that a definition of good agricultural practices appears on page 4137 of the Guidelines as published in the Federal Register.

Dr. Witt asked if there is a difference between good agricultural practices and good agricultural research practices. Dr. Sorensen responded that eventually the two terms would become interchangeable because farmers would be required to keep more and more records.

The Group noted that Appendix 2 had drawn many negative comments from the public. One of the most frequent comments was that Appendix 2 lumped confinement and security measures together. The Group agreed to separate security and confinement measures.

The Group also decided to reorganize Appendix 2 and remove duplications. The Group began by looking at the Good Agricultural Practices section on page 4149, and agreed not to change it. Then the Group edited the first section -- "Domestic, Terrestrial Plants" -- to read as follows:

Confinement Level 1: See Good Agricultural Research Practice.

Confinement Level 2: Should include all Level 1 practices plus one or more of the following, or an equivalent substitute that will reduce the risk to the equivalent of Safety Level 1.

CONFINEMENT MEASURES:

-- Confine all plants to research site.

-- Control seeds, plant stocks, and their movement by wind or water, and secure seeds or plant stocks (Staff note: the Group questioned whether this item should remain.)

-- Exclude birds and other animals.

-- Monitor plants outside research plots.

-- Isolate research site from all cross pollinators.

-- Control pollen (e.g., by male sterility, hand pollination).

-- Destroy plants at termination and fumigate plot to kill seeds or plant parts.

-- Provide isolation distances greater than the distance at which natural pollination has been reported to occur.

-- Provide berms to contain all runoff.

-- Monitor pollen to be collected in the area for genetic markers.

-- Monitor research site for an appropriate length of time after termination of the experiment for genetic escapes. (This does not preclude its use during the monitoring period.)

SECURITY MEASURES:

-- Record all persons entering and leaving the site.

-- Control access.

-- Provide patrolled security.

-- Provide locked security fence.

-- Provide locked fences with alarms.

After the Group finished editing the terrestrial plants section, Dr. Kemp assigned the rewriting of the rest of Appendix 2 as follows:

Domestic, Terrestrial Animals: Dr. Osburn

Microorganisms: Dr. Vidaver

Insects, Nematodes, and Other Arthropods: Dr. Sorensen

Aquatic Animals: Dr. Witt

Aquatic Plants: Dr. Kemp

The Group then discussed the new definitions of safety levels prepared by Ms. Cordle before turning to analysis of the public comments on the Guidelines.

Public Comments

Mr. Stern summarized the OAB staff analysis of the public comments on the Guidelines, which was still in progress.

He said that Appendix 1 had drawn 12 comments, of which 6 discussed the material on attributes. The Group agreed that it already had dealt sufficiently with this issue.

Mr. Stern reported that 16 comments were generally critical of the Guidelines. Most of those comments asked for more direction on what to do and for answers to specific questions. Twenty-five comments were generally supportive of the Guidelines.

Three of the comments generally supported the Guidelines, but called for certain changes. For example, a forester could not relate the plant example in Appendix 1 to the trees with which he worked.

The safety levels drew 25 comments, of which only 1 was supportive. The group agreed it already had addressed that issue.

Appendix 2 drew 50 comments, of which all but 5 were critical. The group agreed it had dealt with most of the concerns in the critical comments. Twenty-one of those comments called for more detail or suggested minor changes.

The issue of classifying modified organisms drew 12 comments: 8 positive and 4 critical. The positive comments recognized the uncertainty inherent in attempting such classifications; one of the negative comments said that too much emphasis had been placed on the parental organism, and that more information was needed on how to classify the modified organism.

The general scenario of the Guidelines drew nine comments, of which one was very critical.

Mr. Stern said that the analysis of the comments was quite difficult because such analysis necessitated subjective judgement, and that comments often had to be taken out of context in order to be quantified. He added that most of the comments had come from the university community.

Dr. Kemp asked if, in light of the comments, the group still was comfortable with the changes it was suggesting. Members expressed continued dissatisfaction with Appendix 1. Dr. Kemp asked if that appendix contained appropriate organisms as examples, and if the examples went far enough.

The Group noted that if the examples went beyond describing the parental organism and were carried through to descriptions of the appropriate confinement level, controversy was likely to follow. For one thing, the Guidelines would, in effect, be recommending or prescribing practices to researchers.

Dr. Kemp asked if five examples in Appendix 1 were sufficient. The group noted that the previous Classification Working Group had developed about 12 examples. Dr. Tolin suggested that the Guidelines be published without the appendices but with a notice saying where examples could be found. Dr. Kemp suggested that the Federal Register contain a separate notice concerning the appendices. Dr. Osburn suggested that all 12 examples be put on the National Biological Impact Assessment Program (NBIAP) Bulletin Board.

Dr. Sorensen suggested that if the levels of safety concern were reduced to three, the examples might not be as necessary. Dr. Vidaver disagreed, saying that the examples illustrated the amount of information needed to comply with the Guidelines, and that the examples provided guidance to the Institutional Biosafety Committees (IBC's).

Dr. Kemp suggested that the five examples remain in the Guidelines, but that a footnote be added to show that additional examples are available. The group agreed to that suggestion.

The group discussed whether a pine tree example should be added.

Dr. Kemp then summarized the changes the group had agreed to: reducing the number of safety levels from five to three, revising the appendices, and interchanging Attributes 1 and 2. Dr. Tolin asked if the number of attributes should be reduced from five to four. Dr. Kemp replied that reduction of the number of attributes may have merit, but that the Group did not want to find itself rewriting the entire document.

Dr. Kemp then thanked the Group for its efforts, and adjourned the meeting at 4:39 p.m.

Susan McCullough, Rapporteur

Daniel Jones, Editor and
Acting Executive Secretary

John Kemp, Chair

* U.S. G.P.O.:1991-311-403:40093/CSRS